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NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4, AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

U.S. patents

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STRUCTURE FILE UPDATES: 4 SEP 2009 HIGHEST RN 1180743-67-2 DICTIONARY FILE UPDATES: 4 SEP 2009 HIGHEST RN 1180743-67-2

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http://www.cas.org/support/stngen/stndoc/properties.html

=> s ibandronic

L1 1 IBANDRONIC

=> d 11

- L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
- RN 114084-78-5 REGISTRY
- ED Entered STN: 23 Apr 1988
- CN Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-(CA INDEX NAME)

OTHER CA INDEX NAMES:

- CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis- (9CI) OTHER NAMES:
- CN BPH 24
- CN Ibandronate
- CN Ibandronic acid
- CN [1-Hydroxy-3-(methylpentylamino)propylidene]diphosphonic acid
- MF C9 H23 N O7 P2
- CI COM
- SR CA

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LC
     STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE,
       IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*,
       PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:
                     WHO
      ОН
                  Ме
H_2O_3P-C-CH_2-CH_2-N-(CH_2)_4-Me
      PO3H2
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
             723 REFERENCES IN FILE CA (1907 TO DATE)
              29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             726 REFERENCES IN FILE CAPLUS (1907 TO DATE)
=> s ibandronic sodium
             1 IBANDRONIC
        344247 SODIUM
L2
             0 IBANDRONIC SODIUM
                 (IBANDRONIC (W) SODIUM)
=> s 138844-81-2
             1 138844-81-2
L3
                 (138844-81-2/RN)
=> s 138926-19-9
             1 138926-19-9
                 (138926-19-9/RN)
=> d 13
L3
    ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN
    138844-81-2 REGISTRY
ED
    Entered STN: 07 Feb 1992
    Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-,
CN
     sodium salt (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
    Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis-,
    monosodium salt (9CI)
OTHER NAMES:
CN
    BM 21.0955
    BM 21.0955Na
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    Bondronat
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    Bondronate
CN
    Boniva
CN
    Bonviva
CN
    Ibandronate sodium
MF
    C9 H23 N O7 P2 . Na
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CI

COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSPATENTS, IMSRESEARCH, MRCK*, PROMT, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

(*File contains numerically searchable property data) CRN (114084-78-5)

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 87 REFERENCES IN FILE CA (1907 TO DATE)
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- 87 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d 2

1 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE The answer numbers requested are not in the answer set. ENTER ANSWER NUMBER OR RANGE (1):end

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- L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
- RN 138926-19-9 REGISTRY
- ED Entered STN: 14 Feb 1992
- CN Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-, sodium salt, hydrate (1:1:1) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis-, monosodium salt, monohydrate (9CI)

OTHER NAMES:

- CN BM 21.0955Na.H20
- CN Ibandronate sodium monohydrate
- CN Monosodium ibandronate monohydrate
- MF C9 H23 N O7 P2 . H2 O . Na
- SR CAS Client Services
- LC STN Files: ADISINSIGHT, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CSCHEM, EMBASE, IMSPATENTS, IMSRESEARCH, MRCK*, PATDPASPC, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

CRN (114084-78-5)

Na

● H2O

25 REFERENCES IN FILE CA (1907 TO DATE)
25 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 24.60 24.82

FULL ESTIMATED COST

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FILE COVERS 1907 - 6 Sep 2009 VOL 151 ISS 11

FILE LAST UPDATED: 4 Sep 2009 (20090904/ED)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2009

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

The ALL, BIB, MAX, and STD display formats in the CA/CAplus family of databases have been updated to include new citing references information. This enhancement may impact record import into database management software. For additional information, refer to NEWS 9.

=> s 13 or 14 87 L3 25 L4 L5 106 L3 OR L4

=> s amorphous

L6 301133 AMORPHOUS

 \Rightarrow s 15 and 16

L7 5 L5 AND L6

=> d 17 fbib ab hitstr 1-5

- L7 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
- AN 2009:876533 CAPLUS
- DN 151:181953
- TI Solid and crystalline ibandronate sodium and processes for preparation thereof
- IN Lifshitz-Liron, Revital; Bayer, Thomas; Aronhime, Judith; Pinchasov, Michael
- PA Teva Pharmaceutical Industries Ltd., Israel
- SO U.S., 32pp., Cont. of U.S. Ser. No. 410,825. now abandoned. CODEN: USXXAM
- DT Patent
- LA English

FAN.CNT 2

| | PAT | CENT : | NO. | | | KIND DATE | | | | | API | | DATE | | | | | | | |
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| PI | | 7563918 20070179119 | | | | B2 A1 | | 2009 2007 | | | US | 2(| 006- | 6445 | 68 | | | 2006 | 12 | 22 |
| | | | | | | | | | | | US | 20 | 004- | 6040 | 26P | | Р | 2004 | 08 | 23 |
| | | | | | | | | | | | US | 2(| 05- | 6908 | 67P | | Р | 2005 | 06 | 16 |
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| | | | IS, | IT, | LI, | LT, | LU, | LV, | MC, | | | | | RO, | • | | SK | , TR | | · |
| | ,,, | | | | | , | , | · | | | • | • | 6040 | • | • | | 2004 | | 23 | |

US 2005-690867P

S 2004-604026P P 20040823 S 2005-690867P P 20050616

EP 2005-791142 A3 20050823

PATENT FAMILY INFORMATION:

FAN 2006:333490

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| | | | | | |
| ΡI | WO 2006024024 | A2 | 20060302 | WO 2005-US30500 | 20050823 |
| | WO 2006024024 | A3 | 20060629 | | |

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DE 202005021414
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                                                              A 20050823
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EP 1930011
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                            20080828
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KR 2007043043
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                                         US 2004-604026P
                                                              P 20040823
                                         US 2005-690867P
                                                              Ρ
                                                                 20050616
                                         WO 2005-US30500
                                                              W 20050823
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AB The present invention relates to solid amorphous and crystalline forms of ibandronate sodium. Thus, a solution of NaOH (0.63 g) in water/isopropanol (IPA) was added dropwise to a solution of amorphous ibandronic acid (5 g) in water/IPA at reflux temperature, and the reaction mixture

maintained at reflux temperature for 4 h to obtain a pH of 3.93-4.01. The reaction mixture was then cooled to room temperature, stirred for 72 h, and further cooled using an ice-bath. The precipitate was filtered, washed, and dried in a vacuum oven at 50° to give 4.4 g of ibandronate sodium crystal form F.

IT 138844-81-2P, Ibandronate sodium

RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation of solid amorphous and crystalline ibandronate sodium)

RN 138844-81-2 CAPLUS

CN Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-, sodium salt (1:1) (CA INDEX NAME)

Na

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:724495 CAPLUS

DN 147:125584

TI Novel polymorphic forms of ibandronate for tablets

IN Reddy, Muddasani Pulla; Usharani, Vattikuti; Chowdary, Nannapaneni Venkalah

PA Natco Pharma Limited, India

SO PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATEN: | NO. | | | KIND DATE | | | 1 | APPL | | DATE | | | | | | |
|----|--------|--------------------------|-----|-----|----------------------------|-----|-----|-----|------|------|------|----------|-----|-----|-----|-----|-----|
| PI | | 2007074475 2007074475 | | | A2 20070705 A3 20070907 | | | 1 | WO 2 | 006- | | 20061221 | | | | | |
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| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FΙ, | GB, | GD, |
| | | GE, | GH, | GM, | GT, | HN, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | KM, | KN, |
| | | KP, | KR, | KΖ, | LA, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | LY, | MA, | MD, | MG, | MK, |
| | | MN, | MW, | MX, | MY, | MZ, | NA, | NG, | ΝI, | NO, | NΖ, | OM, | PG, | PH, | PL, | PT, | RO, |
| | | RS, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SM, | SV, | SY, | ТJ, | TM, | TN, | TR, | TT, |
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| | | IS, | ΙΤ, | LT, | LU, | LV, | MC, | NL, | PL, | PT, | RO, | SE, | SI, | SK, | TR, | BF, | ВJ, |
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| | | KG, | KΖ, | MD, | RU, | ТJ, | TM, | AP, | EA, | EP, | OA | | | | | | |

IN 2005-CH1936 A 20051227

IN 2005-CH1936 IN 2005CH01936 20070720 Α 20051227 AB The present invention relates to novel and stable polymorphic forms of ibandronate monosodium monohydrate and processes for their preparation and pharmaceutical compns. containing them, such as tablets. Ibandronate monosodium monohydrate is useful as bone resorption inhibitor. The novel crystalline forms are designated as Form I, Form II and the amorphous ibandronate monosodium monohydrate as Form III. Thus, the reaction of 100 q of 3-(N-methyl-N-pentylamino) propionic acid-HCl and 49 q of crystalline phosphorous acid at 75°, followed by the addition of phosphorous trichloride and adjusting the pH to 4.3-4.4 using NaOH yielded 145 g of ibandronate. Ibandronate prepared (25 g) was dissolved in 200 mL of water, water was distilled of from the reaction mass and 100 mL of fresh water was added. The reaction mass was treated with 2 g of carbon and filtered. To the filtrate 200 mL of acetone were added at $50\text{--}60^{\circ}$ resulting in immediate crystallization of ibandronate. The reaction mass was cooled to 25° and maintained for 1 h before filtration. The wet solid was washed with acetone and dried at 60° to get 20 g of Form I crystals of ibandronate monosodium monohydrate. Form I crystals of ibandronate monosodium monohydrate prepared were formulated into tablets containing

to 150 mg of ibandronic acid per single dosage unit.

IT 138926-19-9P, Ibandronate sodium monohydrate

RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation of polymorphic forms of ibandronate monosodium monohydrate for tablets)

RN 138926-19-9 CAPLUS

equivalent

CN Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-, sodium salt, hydrate (1:1:1) (CA INDEX NAME)

Na

● H2O

OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:333490 CAPLUS

DN 144:338225

TI Preparation of solid and crystalline ibandronate sodium

IN Lifshitz-Liron, Revital; Bayer, Thomas; Aronhime, Judith

PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.

SO PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DT Patent LA English FAN.CNT 2

| FAN. | | 2 IENT N | Ο. | | | KIND DATE | | | | | API | PLI | DATE | | | | | | | |
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| PI | | 20060 20060 | | | | A2 A3 | _ | 2006 2006 | | | WO | 20 | | 2 | 0050 | 823 | | | | |
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| | | | | | | | | | | | US | 20 | 05- | 6040 6908 | 67P | | P 20040823 P 20050616 | | | |
| | | 25766 | | A1 | | 2006 | | CA 2005-2576659 US 2004-604026P US 2005-690867P WO 2005-US30500 | | | | | | | 20050823 P 20040823 P 20050616 W 20050823 20050823 | | | | | |
| | EP | | AT, IE, | SI, | | LV, | DK, | 2006 ES, RO, | FR, | GB, CY, | GI AI | ₹, | IT, TR, | BG, | LU, CZ, | EE, | SE, HU, | MC, PL, | PT, SK, | |
| | .TP | 2007512237 | | | | T | | 2007 | 0517 | | US WO | 20 20 |)05-)05- | 6040 6908 US30 5369 | 67P 500 | | P 2 W 2 | 0040 0050 0050 0050 | 616 823 | |
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| | DE | 20200 | | U1 | | 0424 | | DE US US | 20 20 20 | 05- 04- 05- | | 0502 26P 67P | 1414 | 2 P 2 P 2 | 0050 0050 0040 0050 0050 | 823 823 616 | | | | |
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| | | | IS, | IT, | LI, | LT, | LU, | LV, | MC, | | US US | 20 20 |)04-)05- | RO, 6040 6908 7911 | 26P 67P | | P 2 P 2 | TR 0040 0050 0050 | 616 | |
| | IN | 2007DN00555 | | | | A | | 2007 | 0817 | | IN US | 20 20 | 007- 004- | DN55 6040 US30 | 5 26P | | 2 P 2 | 0070 0040 0050 | 122 823 | |
| | MX | 20070 | 36 | | A | | 2008 | 0828 | | US | 20 | 004- | 2286 6040 6908 | | | P 2 | 0070 0040 0050 | 823 | | |

| | KR 2007 | 70430 | 43 | | А | | 2007 | 0424 | I U | KR JS | 2005-U 2007-7 2004-6 | 7059 5040 | 22 26P | | W P | | 314 |
|-------------|--------------------|-------|------|-------|------|------|------|------|--------|-----------------|----------------------------|--------------|-----------|------|--------|----------------|------|
| | | | | | | | | | | | 2005-6 2005-t | | | | | 20050 20050 | |
| PATE FAN | NT FAMIL 2009:87 | | | ATIO: | N: | | | | V | VO | 2005 (| | 300 | | VV | 20030 | 025 |
| | PATENT | | | | KINI | | DATE | | | APPLICATION NO. | | | | | | DATE | |
| ΡI | US 7563 US 2007 | | | | В2 | | | | | JS | 2006-6 | 6445 | 68 | | - | 20061 | .222 |
| | | | | | | | | | J | JS | 2004-6 | 5040 | 26P | | Р | 20040 | 823 |
| | | | | | | | | | | | 2005-6 | | | | | | |
| | | | | | | | | | J | JS | 2005-2 | 2110 | 62 | | В1 | 20050 | 823 |
| | | | | | | | | | J | JS | 2006-4 | 1108 | 25 | | В1 | 20060 | 424 |
| | DE 2020 | 0502 | 1414 | | U1 | | 2008 | 0424 | Ι | DΕ | 2005-2 | 2020 | 0502 | 1414 | 1 | 20050 | 823 |
| | | | | | | | | | | | 2004-6 | | | | | 20040 | |
| | | | | | | | | | J | JS | 2005-6 | 5908 | 67P | | Р | 20050 | 616 |
| | | | | | | | | | | | 2005-7 | | | | | | |
| | EP 1930 | 011 | | | A2 | | 2008 | 0611 | Е | ΞP | 2008-2 | 2626 | | | | 20050 | 823 |
| | EP 1930 | 011 | | | А3 | | 2008 | 0618 | | | | | | | | | |
| | R: | | | | | | | | | | E, ES, L, PT, | | | | | | IE, |
| | | | | | | | | | | | 2004-6 | | | | | | 823 |
| | | | | | | | | | | | 2005-6 | | | | | | |
| | | | | | | | | | E | ΞP | 2005-7 | 7911 | 42 | | АЗ | 20050 | 823 |
| AB | The pre | sent | inv | enti | on r | elat | es t | o so | lid a | amo | orphous | an | d cr | ysta | all: | ine | |
| | forms c | of ib | andr | onat | e so | dium | . T | hus, | ibar | ndı | conate | sod | ium | was | dia | ssolve | d in |

DMSO and 1-butanol was added to it, and the precipitate was isolated by vacuum filtration, washed with 1-butanol and dried at 50° to obtain

ibandronate sodium crystal form C.

138844-81-2P ΙT

> RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of solid amorphous and crystalline forms of ibandronate

sodium)

138844-81-2 CAPLUS RN

Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-, CN sodium salt (1:1) (CA INDEX NAME)

● Na

OSC.G THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS) RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

2006:11476 CAPLUS ΑN

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DN 144:94242
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- TI Solid and crystalline ibandronic acid
- IN Bayer, Thomas; Dolitzky, Ben-Zion; Lifshitz-Liron, Revital; Perutski, Inna; Pinchasov, Michael
- PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical USA, Inc.
- SO PCT Int. Appl., 67 pp. CODEN: PIXXD2
- DT Patent

| DT | | tent | | | | | | | | | | | | | | | | | |
|------|-----|---|-------------------|-------------------|-------------------|-------------------|-------------------|---|-------------------|----------------------|---|----------------------------------|-------------------------|--|--|---|----------------------------------|-------------------|--|
| LA | | glish | | | | | | | | | | | | | | | | | |
| FAN. | | TENT | | | | KINI | | DATE | | | APPI | ICAT | ION I | .00 | | Γ | DATE | | |
| ΡI | | 2006 2006 | 0023 | | | A2 A3 | | 2006 2006 | 0105 | | WO 2 | 2005- | US22 | 20050623 | | | | | |
| | ,,, | W: | AE, CN, GE, | AG, CO, GH, | CR, GM, | AM, CU, HR, | AT, CZ, HU, | AU, DE, ID, | AZ, DK, IL, | DM, IN, | DZ, IS, | EC, | EE, KE, | EG, KG, | ES, KM, | FI, KP, | CA, GB, KR, MZ, | GD, KZ, | |
| | | NG, NI, NO SL, SM, S ZA, ZM, Z | | SY, | | | | | | | | | | | | | | | |
| | | RW: | IS, CG, KE, | IT, CI, LS, | LT, CM, MW, | LU, GA, MZ, | MC, GN, NA, | NL, GQ, | PL, GW, | PT, ML, | RO, MR, | SE, NE, | SI, SN, | SK, TD, | TR, TG, | BF, BW, | HU, BJ, GH, BY, | CF, GM, | |
| | | KZ, MD, RU | | | | TJ, | TM | | | | US 2 | 2004- 2004- 2005- | 6200 | P 20040623 P 20041018 P 20050616 | | | | | |
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| | EP | 1687007 R: AT, BE, CH, IE, SI, LT, BA, HR, IS, | | LT, | LV, | DK, | | FR, | GB, CY, | GR, AL, | TR, | LI, BG, | LU, CZ, | | SE, HU, | PL, | PT, SK, | | |
| | | 0000 | 0.1.5.1 | | | | | 0000 | 0510 | | US 2 US 2 WO 2 | 2004- 2004- 2005- | 6200: 6908: US22: | 16P 68P 410 | | P 2 P 2 W 2 | 20040 20041 20050 20050 | 018 616 623 | |
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| | | 7311174 | | | | | | | | | US 2 US 2 US 2 | 2004- 2005- 2005- 2006- | 6200: 6908: 1654: | | P 20040623 P 20041018 P 20050616 B1 20050622 B1 20060112 | | | | |
| | IN | 2006DN07758 | | | | A | | 2007 | 0817 | | US 2 | 2006- 2004- 2005- | 5825 | 00P | | P 2 | 20061 20040 20050 | 623 | |
| | MX | 2007000087 | | А | | 2007 | 1106 | WO 2005-US22410 MX 2007-87 US 2004-582500P US 2004-620016P US 2005-690868P WO 2005-US22410 | | | | | | P 2 P 2 P 2 | 20061 20040 20041 20050 | 220 623 018 616 | | | |
| | US | 3 20090023949 | | | | A1 | | 2009 | 0122 | | | 2008- | | | , | | 20030 | | |

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AB Provided are novel crystalline and amorphous forms of ibandronic acid, methods for their preparation, and pharmaceutical compns. containing them.

Also provided are methods for purifying and assaying ibandronic acid in any crystalline form (or amorphous). Amorphous ibandronic acid was prepared by drying a solution and a crystal form S1 prepared from the amorphous form by adding acetone to a solution

IT 138844-81-2P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (solid and crystalline ibandronic acid)

RN 138844-81-2 CAPLUS

CN Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-, sodium salt (1:1) (CA INDEX NAME)

Na

OSC.G 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:612312 CAPLUS

DN 143:97528

TI An improved process for the preparation of alkyl- and aryl-substituted $\alpha\text{-hydroxy-1,1--ethanediphosphonic}$ acids and salts thereof by solvent-free reaction of carboxylic acids with phosphorous acid and phosphorus oxychloride

IN Grassi, Simona; Volante, Anna

PA Lyogen Limited, Cyprus

SO PCT Int. Appl., 9 pp.

CODEN: PIXXD2
DT Patent

LA English

FAN.CNT 1

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PATENT NO.
                  KIND DATE APPLICATION NO. DATE
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                                                                _____
    WO 2005063779
                                                                20041222
                       A2 20050714
                                         WO 2004-EP14556
PΤ
    WO 2005063779
                       A3 20050929
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
            RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
            MR, NE, SN, TD, TG
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                                                          W 20041222
                                          WO 2004-EP14556
    EP 1716161
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                               20061102
                                          EP 2004-804152
                                                                 20041222
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
                                          IT 2003-MI2582 A 20031223
                                          IT 2004-MI80
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                                                            W 20041222
                                          WO 2004-EP14556
    US 20070112197
                         Α1
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                                                           A 20031223
                                          IT 2003-MI2582
                                          IT 2004-MI80
                                                            A 20040122
                                          WO 2004-EP14556
                                                            W 20041222
    CASREACT 143:97528; MARPAT 143:97528
OS
    \alpha-Hydroxy-1,1-ethanediphosphonic acids R(CH2)mC(OH)[PO(OH)2]2 [m =
AΒ
    1-8; R = dialkylamino or 5- or 6-membered (hetero)aryl, preferably
    imidazolyl and pyridinyl], preferably risedronic, zoledronic and
    ibandronic acids, useful in therapy as inhibitors of bone reabsorption (no
    data) were prepared by reaction carboxylic acids R(CH2)mCOOH (same m, R)
    with 2-4 equiv of POC13 and 8-12 equiv of H3PO3, preferably the carboxylic
    acid:POCl3:H3PO3 ratio is 1:3:10. In an example, addition of 0.19 mol of
    POC13 to a mixture of 0.06 mol of (3-pyridinyl)acetic acid and 0.58 mol of
    H3PO3 followed by stirring at 60-70^{\circ} for 24 h with subsequent aqueous
    work-up gave 1-hydroxy-2-(3-pyridinyl)-1,1-ethanediphosphonic acid
    (risedronic acid) in 60% yield. Amorphous monosodium salt of
    1-hydroxy-2-[(methyl)(pentyl)amino]-1,1-1,1-ethanediphosphonic acid
    (monosodium ibandronate), useful in the pharmaceutical use due of its
    increased bioavailability (no data) was prepared by neutralization of 10 g
    of analogously prepared ibandronic acid in 200 mL of water by 1M NaOH to pH
    4.3-4.4 and lyophilization of the resulting solution
    138844-81-2DP, amorphous
ΙT
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (improved process for preparation of \alpha-hydroxy-1,1-ethanediphosphonic
       acids by solvent-free phosphonation of carboxylic acids by phosphorous
       acid and phosphorus oxychloride)
    138844-81-2 CAPLUS
RN
    Phosphonic acid, P,P'-[1-hydroxy-3-(methylpentylamino)propylidene]bis-,
CN
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sodium salt (1:1) (CA INDEX NAME)

● Na

OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
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